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Why ribonucleases induce tumor cell death

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Abstract

The characteristics and the possible mechanisms of action of cytotoxic ribonucleases (RNases), promising antitumor drugs, are described. Original experimental data and the results of analysis of recent publications have made it possible to identify the cellular components providing for the selective effects of exogenous RNases on tumor cells, on the one hand, and to estimate the contributions of individual molecular determinants to the enzyme cytotoxicity, on the other hand. The predominant effect of the electric charge of the RNase molecule on the induction of cell death has been demonstrated. The cytotoxic effects of RNases are determined by the catalytic cleavage of accessible RNA, the action of the products of its hydrolysis, and the noncatalytic electrostatic interaction of the exogenous enzyme with cell components. Potential RNase targets in a tumor cell and the role of modulation of calcium-dependent potassium channels and the ras oncogene in RNase-induced cell damage are considered. The effect of cytotoxic RNases on gene expression by affecting RNA interference is discussed. © 2005 Pleiades Publishing, Inc.

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Keywords

Antitumor activity, Catalytic activity, Charge, Cytotoxicity, KCa channels, Ras, Ribonucleases, RNA interference, Stability, Structure